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- (74) Agents: BOUDREAU, William, R. et al.; Eli Lilly And Company, P. O. Box 6288, Indianapolis, IN 46206-6288 (US).
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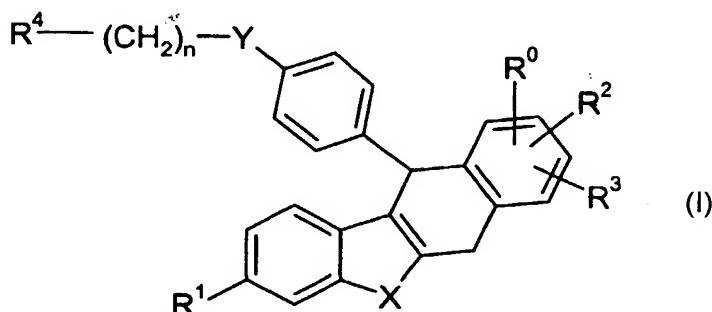
## Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY,

[Continued on next page]

- (54) Title: DERIVATIVE OF DIHYDRO-DIBENZO (A) ANTHRACENES AND THEIR USE AS SELECTIVE ESTROGEN RECEPTOR MODULATORS



(57) Abstract: The present invention provides a compound of the formula (I) wherein R<sup>1</sup> is -H, -OH, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), -OCOC<sub>6</sub>H<sub>5</sub>, -OCO(C<sub>1</sub>-C<sub>6</sub> alkyl), or -OSO<sub>2</sub>(C<sub>2</sub>-C<sub>6</sub> alkyl); R<sup>0</sup>, R<sup>2</sup> and R<sup>3</sup> are each independently -H, -OH, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), -OCOC<sub>6</sub>H<sub>5</sub>, -OCO(C<sub>1</sub>-C<sub>6</sub> alkyl), -OSO<sub>2</sub>(C<sub>2</sub>-C<sub>6</sub> alkyl) or halo; R<sup>4</sup> is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-hexamethyleneimino; n is 2 or 3; X is S- or -HC=CH-; and Y is O-, -S-, -NH-, -NMe-, or -CH<sub>2</sub>-; or a pharmaceutically acceptable salt thereof; pharmaceutical compositions thereof,

optionally in combination with estrogen and progestin; methods of inhibiting a disease associated with estrogen deprivation; and methods for inhibiting a disease associated with an aberrant physiological response to endogenous estrogen.

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CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG,  
CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)  
— of inventorship (Rule 4.17(iv)) for US only

— before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

**Published:**

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 03/26304

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C07D409/12 C07D295/08 A61K31/381 A61K31/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GRESE T A ET AL: "STRUCTURE-ACTIVITY RELATIONSHIPS OF SELECTIVE ESTROGEN RECEPTOR MODULATORS: MODIFICATIONS TO THE 2-ARYLBENZOTHIOPHENE CORE OF RALOXIFENE" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 40, no. 2, 17 January 1997 (1997-01-17), pages 146-167, XP002050782 ISSN: 0022-2623 page 152; table 3 compound 131	29
X	EP 0 759 434 A (LILLY CO ELI) 26 February 1997 (1997-02-26) examples 10,11 claim 1	29-32 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed Invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed Invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

13 January 2004

Date of mailing of the International search report

05/02/2004

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/03/26304

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 761 669 A (LILLY CO ELI) 12 March 1997 (1997-03-12) page 3, line 3-8 claim 1 -----	1-47
A	WO 02 16316 A (MESTRES JORDI ;AKZO NOBEL NV (NL); LOOZEN HUBERT JANJOZEF (NL); VE) 28 February 2002 (2002-02-28) page 1, line 4-9 claim 1 -----	1-47

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 17-28 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

# INTERNATIONAL SEARCH REPORT

International Application No.  
/US 03/26304

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
**see FURTHER INFORMATION sheet PCT/ISA/210**
2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2003/26304

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 0759434	A	26-02-1997	AU CA EP JP WO US	6774096 A 2228997 A1 0759434 A1 11511169 T 9706796 A1 5728724 A	12-03-1997 27-02-1997 26-02-1997 28-09-1999 27-02-1997 17-03-1998
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